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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
MEAH, MOHAMMAD Y	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 05/04/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/525,674	KROGER ET AL.	
	Examiner	Art Unit	
	Mohammad Meah	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 February 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12 and 14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12 and 14* is/are rejected.

7)☒ Claim(s) *4-6,11 and 12* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *02/24/05, 12/5/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

DETAILED ACTION

Applicant, on date 2/13/2006 elected with traverse Group I (claims 1—12, 14), Protein SEQ NO: 2 or DNA SEQ ID NO: 1 and lysC gene for examination. Applicant withdrew claim 13.

Election/Restriction

Applicant, on date 2/13/2006 elected with traverse Group I (claims 1-12 and 14) drawn to methods of fermentative production of sulfur containing compound by using coryneform bacteria comprising metA active gene of SEQ ID NO:1 for examination and further selected lysC gene from claim 12. Groups II (claims 15-16) and claim 13 of group I of election/restriction-office action of date 012/23/2005 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected Groups.

The traversal is on the ground(s) that there is a lack of unity exit between the claims and therefore restriction was not proper. Applicant's arguments have been fully considered but are not deemed persuasive to withdraw the restriction requirement previously applied as explained bellow:

1. Applicants argument of the claims are linked by a special technical feature is not persuasive because Lorbert et al. (US 60485564) teaches method for fermentation of L-methionine using corynebacterium having plasmid containing metA. Lorbert et al. (US 60485564) is a prior art because it is filed before applicant PCT filing date. Applicant's foreign filing date is not valid unless proper translation is submitted. Further evidence that the claims lack special technical feature is found in rejection heading under U.S.C.102 below.

2. Applicants further argue that use of gene or protein having no special technical feature posses special technical feature and there would be no undue burden on the examiner to examine claims directed to methods of using either different DNAs encoding metA proteins comprising different SEQ IDS or different genes. This is not persuasive because if gene or protein does not posses special technical feature, method of using them as disclosed in claim 1 also does not posses special technical feature. Furthermore while the search for each of these distinct groups would be overlapping it would not be coextensive. Art that applies for one protein of specific SEQ ID or gene may or may not be relevant to the others.

3. With regard to the finding of unity of invention in the international phase, it is noted that even if the International Authority found unity of invention regarding the instant claims, according to 37 CFR 1.499, if the Examiner finds that a national stage application lacks unity of invention under 37 CFR 1.475, the Examiner may in an Office action require the applicant in the response to that action to elect an invention to which the claims shall be restricted. Such requirement may be made before any action on the merits but may be made at any time before the final action at the discretion of the

Examiner. Thus a finding of unity of invention in the international stage is not binding on the examination during national phase examination.

Therefore the restriction is maintained and final.

Priority

Acknowledgement is made of applicant's priority date based on application filing date of 08/26/2003 for Application No. PCT/EP03/ 09452.

Objections

Claims 4-6, 11-12 are objected to comprising on non-elected subject matters.

An appropriate correction is required.

Claim Rejections

35 U.S.C 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 5-6 and 11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The terms "homologous" in claims 5-6 are indefinite, broad and confusing as it is unclear as how similar to a specific sequence homologous is?

Claim 11- the recitation " is at least particularly switched off" makes the claim unclear because the recited phrase is non-standard jargon. Is this synonymous with eliminated?

Claims 1-12 and 14 are rejected under U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor at the time the application was filed, had possession of the claimed invention.

Claims 1, 3-12 and 14 are directed to methods of preparation of any sulfur containing chemical using microorganism expressed with any polynucleotide encoding protein having metA activity. The specification fails to describe in any fashion the physical and/or chemical properties of the claimed class of sulfur containing chemical, which can be produced by the instant methods. Given this lack of description of representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Claims 1-12 and 14 are directed to methods of preparation of sulfur containing chemical using microorganism expressing a genus of polynucleotide encoding metA protein. The specification teaches the structure of only a few representative species of such polynucleotids (SEQ ID NO: 1, 3, 4---- 45). Moreover, the specification fails to describe any other representative species by any identifying characteristics or

properties other than the functionality of encoding a protein with metA activity. Given this lack of description of representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention. Claims 10-12 further directed to methods of preparation of sulfur containing chemical using microorganism comprising additionally one of any gene of the biosynthetic pathway is modulated in addition of any metA gene. The specification fails to describe all such genes, which can be so modified, and what modifications of any other gene of the biosynthetic pathway result in the desired result, i.e., its activity is not influence the metabolic pathway. Furthermore, the specification fails to describe all methods of reducing expression of a gene which reduce the production of sulfur containing chemicals as the specification fails to describe which genes can be modified and how they can be modified to produce the desired results.

Claims 1-12, 14 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of preparation of L-methionine using corynebacterium microorganism expressing a polynucleotide of SEQ ID NO: 1 does not reasonably provide enablement for preparation of any sulfur containing chemical using microorganisms expressing any polynucleotide encoding a metA protein. The claims broadly recite using a corynebacterium expressing any heterologous metA gene to produce a genus of fermentation products. The specification fails to describe how microorganism expressed with these polynucleotides produce any fermentation product.

Claims 1-12, 14 are so broad as to encompass methods of using any microorganism expressing a heterologous gene encoding a metA protein to produce any sulfur-containing chemical.

Claims 10-12 are so broad as to encompass methods of using any microorganism expressing with any other gene of the biosynthetic pathway of said sulfur-containing compound in addition of the polynucleotide encoding the metA protein to produce any sulfur-containing chemical or methods of using corynebacteria in which any metabolic pathway which reduces production of sulfur compound is reduced or eliminated. The specification fails to describe how any other gene of the biosynthetic pathway of said sulfur compound can be modified such that its activity is not influence by metabolites of the metabolic pathway and how to reduce expression of any gene which encodes a protein which reduces the production of sulfur containing chemicals.

The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to all metA encoding polynucleotides and use of any other gene of the biosynthetic pathway of said sulfur compound broadly encompassed by the methods of production any sulfur containing chemical described in the claims nor for all methods of altering metabolic pathways which degrade the desired sulfur compound. Since the nucleic acid sequence of a DNA determines its structural and functional properties, predictability of which changes can be tolerated in a DNA's nucleic acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which nucleotides of polynucleotide's nucleic acid sequence, if any, are

tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the polynucleotide's structure relates to its function. However, in this case the disclosure is limited to a few polynucleotides of SEQ ID NO: 1, 2, -etc. While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a polynucleotide's sequence where nucleic acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any polynucleotide and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given polynucleotide to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass methods of using microorganisms expressing any metA gene with polynucleotide to produce any sulfur containing chemical because the specification does **not** establish: (A) polynucleotide structure of metA gene which may be modified without effecting metA activity; and modification of polynucleotide structure of any other gene of microorganism's biosynthetic pathway without effecting the production of sulfur containing chemical (B) the general tolerance of metA activity to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any polynucleotide residues with an expectation of obtaining the desired biological function;

and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including methods of using any polynucleotide with an enormous number of nucleic acids encoding protein having metA activity. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of polynucleotide for the use in the claimed methods having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

CLAIM Rejection - 35 U.S.C 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, 7-12 and 14 are rejected under 35 U.S.C. 102(b) as being anticipated by Bathe et al. (US 2002/0110877).

Bathe et al. teaches isolation of polynucleotide (SEQ ID NO: 1) encoding metA protein of SEQ ID NO: 2 (claim 1) from Corynebacterium and expression of the said metA gene in host cells like, E. coli, Corynebacterium glutamicum, etc via expression vector and/ or integration of the bacterial chromosome by said gene, processes of production of L-methionine using fermentation process comprising Corynebacterium (including Corynebacterium glutamicum ATCC13032) overexpressed with metA genes (claim 1 and 19) and isolation of sulfur –containing chemicals. Furthermore Bathe et al teaches processes of production of L-methionine using Corynebacterium (Corynebacterium glutamicum) overexpressed with metA gene and additionally another gene overexpressed or mutated including LysC gene (claim 23). Additionally Bathe et al teaches processes of production of L-methionine using Corynebacterium (Corynebacterium glutamicum) overexpressed with metA gene and has reduced expression of one or more biosynthetic pathway polypeptide genes (such as gene of Homoserine kinase, threonine dehydratase, etc, (claim 24)).

Claims 5-6 are rejected under 35 U.S.C. 102(b) as being anticipated by Bathe et al. (US 2002/0110877). Bathe et al. teaches method of production of sulfur-containing compound using fermentation process comprising Corynebacterium expressed with polynucleotide (SEQ ID NO: 1) encoding metA protein of SEQ ID NO: 2. While the metA polynucleotide (SEQ ID NO:1) encoding metA protein of SEQ ID NO:2 of Bathe is not 100% identical to that of metA polynucleotide sequences of present application, they are homologous to the metA genes of the present application, since Bethe's

polynucleotide (SEQ ID NO:1) encoding metA protein of SEQ ID NO:2 shows MetA activity.

Applicant's gene comprising SEQ ID NO: 1 encoding metA protein of SEQ ID NO:2 appears to be novel. Therefore, method of producing L-methionine using Corynebacterium diphteriae having metA-encoding gene of SEQ ID NO:1 will be allowable.

]Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mohammad Meah whose telephone number is 571-272-1261. The examiner can normally be reached on 8:30-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 571-272-0928. The fax

phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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Examiner, Art Unit 1652

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